CLAIMS

1. A method of preparing a substituted tetracycline compound, comprising contacting a reactive tetracycline chemical complex comprising a reactive tetracycline-based precursor compound and a transition metal catalyst; forming a reactive chemical intermediate with a reactive organic substituent precursor under appropriate conditions, such that a substituted tetracycline compound is formed.

2. A method of preparing a substituted tetracycline compound, comprising combining a reactive tetracycline-based precursor compound and a reactive organic substituent precursor in the presence of a transition metal catalyst under appropriate conditions, such that a substituted tetracycline compound is formed.

3. The method of claim 1 or 2, wherein said transition metal catalyst comprises rhodium, iron, iridium, chromium, zirconium, nickel, copper, palladium, or mixtures thereof..

4. The method of claim 3, wherein said transition metal catalyst comprises palladium acetate, $Pd(PPh_3)_4$, $Pd(AsPh_3)_4$, $PdCl_2(PhCN)_2$, $PdCl_2$ $(Ph_3P)_2$, $Pd_2(dba)_3$-$CHCl_3$; or combinations thereof.

5. The method of claim 1 or 2, wherein said reactive tetracycline-based precursor compound is selected from the group consisting of oxytetracycline; chlortetracycline; demeclocycline; doxycycline; chelocardin; minocycline; roliteteracycline; lymecycline; sancycline; methacycline; apicycline; clomocycline; guamecycline; meglucycline; mepylcycline; penimepicycline; pipacycline; etamocycline; and penimocycline arenediazonium salts, iodo derivatized tetracycline compounds, or boronic acid derivatized tetracycline compounds.

6. The method of claim 1 or 2, wherein said reactive tetracycline-based precursor compound is selected from the group consisting of reactive minocycline-based precursor compounds, reactive doxycycline-based precursor compounds, and reactive sancycline-based precursor compounds.

7. The method of claim 1 or 2, wherein said reactive organic substituent precursor is carbon monoxide.

8. The method of claim 7, wherein said method further comprises contacting the reactive chemical intermediate with an additional reactive organic substituent precursor.

9. The method of claim 8, wherein said additional reactive organic substituent precursor is an amide precursor, a ester precursor, an anhydride precursor, a hydrazone precursor, an imide precursor, a ketone precursor, or a nitrile precursor.

10. The method of claim 9, wherein said amide precursor is an amine.

11. The method of claim 9, wherein said ester precursor is an alcohol.

12. The method of claim 1, wherein said substituted tetracycline compound is substituted at the 9 position.

13. The method of claim 1, wherein said substituted tetracycline compound is substituted at the 7 position.

14. A 7-substituted tetracycline compound, wherein the substituent at the 7 position is connected with a -C-C- linkage and comprises a carbonyl moiety.

15. The 7-substituted tetracycline compound of claim 14, wherein said carbonyl moiety comprises an amide, an ester, a ketone, an anhydride, a hydrazone moiety, an imide, or a nitrile.

16. The 7-substituted tetracycline compound of claim 15, wherein said carbonyl moiety is an alkyl ester.

17. The 7-substituted tetracycline compound of claim 15, wherein said carbonyl moiety is a ketone.

18. The 7-substituted tetracycline compound of claim 17, wherein said ketone is a diketone.

19. The 7-substituted tetracycline compound of claim 15, wherein said carbonyl moiety is an amide.

20. The 7- substituted tetracycline compound of claim 15, wherein said compound is 7-sancycline methyl ester, 7-sancycline butyl ester, 7-(2'-N', N'-dimethylaminoethane-1',2'-dione)-sancycline, 7-(morpholin-4'-yl-ethane-1',2'-dione)-sancycline, or 7-(N',N'-dimethylbenzamide) sancycline.

21. A 9-substituted tetracycline compound, wherein the substituent at the 9 position is connected with a -C-C- linkage and comprises a carbonyl moiety.

22. The 9-substituted tetracycline compound of claim 21, wherein said carbonyl moiety comprises an amide, an ester, a ketone, an anhydride, a hydrazone moiety, an imide, or a nitrile.

23. The 9-substituted tetracycline compound of claim 22, wherein said carbonyl moiety is an alkyl ester.

24. The 9-substituted tetracycline compound of claim 22, wherein said carbonyl moiety is a ketone.

25. The 9-substituted tetracycline compound of claim 24, wherein said ketone is a diketone.

26. The 9-substituted tetracycline compound of claim 22, wherein said carbonyl moiety is an amide.

27. The 9-substituted tetracycline compound of claim 22, wherein said compound is 9-(morpholin-4'-yl-methanone) sancycline, 9 sancycline methyl ester, and 9-sancycline butyl ester.

28. A substituted tetracycline compound, made by a method comprising contacting a reactive tetracycline chemical complex comprising a reactive tetracycline-based precursor compound and a transition metal catalyst; forming a reactive chemical intermediate with a reactive organic substituent precursor under appropriate conditions, such that a substituted tetracycline compound is formed.

29. The substituted tetracycline compound of claim 28, wherein said transition metal catalyst comprises rhodium, iron, iridium, chromium, zirconium, nickel, copper, palladium, or mixtures thereof.

30. The substituted tetracycline compound of claim 29, wherein said transition metal catalyst comprises palladium acetate, $Pd(PPh_3)_4$, $Pd(AsPh_3)_4$, $PdCl_2(PhCN)_2$, $PdCl_2$ $(Ph_3P)_2$, $Pd_2(dba)_3$-$CHCl_3$; or combinations thereof.

31. The substituted tetracycline compound of claim 28, wherein said reactive tetracycline-based precursor compound is selected from the group consisting of oxytetracycline; chlortetracycline; demeclocycline; doxycycline; chelocardin; minocycline; roliteteracycline; lymecycline; sancycline; methacycline; apicycline; clomocycline; guamecycline; meglucycline; mepylcycline; penimepicycline; pipacycline; etamocycline; and penimocycline arenediazonium salts, iodo derivatized tetracycline compounds, or boronic acid derivatized tetracycline compounds.

32. The substituted tetracycline compound of claim 31, wherein said reactive tetracycline-based precursor compound is selected from the group consisting of reactive minocycline-based precursor compounds, reactive doxycycline-based precursor compounds, and reactive sancycline-based precursor compounds.

33. The substituted tetracycline compound of claim 28, wherein said reactive organic substituent precursor is carbon monoxide.

34. The substituted tetracycline compound of claim 28 or 33, wherein said method further comprises contacting the reactive chemical intermediate with an additional reactive organic substituent precursor.

35. The substituted tetracycline compound of claim 34, wherein said additional reactive organic substituent precursor is an amide precursor, a ester precursor, an anhydride precursor, a hydrazone precursor, an imide precursor, a ketone precursor, or a nitrile precursor.

36. The substituted tetracycline compound of claim 35, wherein said amide precursor is an amine.

37. The substituted tetracycline compound of claim 35, wherein said ester precursor is an alcohol.

38. The substituted tetracycline of claim 28, wherein said substituted tetracycline compound is substituted at the 9 position.

39. The substituted tetracycline of claim 28, wherein said substituted tetracycline compound is substituted at the 7 position.